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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/601,777	06/24/2003	Tadashi Okamoto	03560.003310.	9502

5514 7590 05/24/2005

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EXAMINER	
DEJONG, ERIC S	

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 05/24/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/601,777	OKAMOTO ET AL.	
	Examiner	Art Unit	
	Eric S. DeJong	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 April 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18 and 20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-20* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/~~Mail Date~~ 1sheet
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election of the invention of Group I (claims 1-18 and 20) in the reply filed on 07 April 2005 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claim 19 is withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 07 April 2005.

Claims 1-18 and 20 are currently under examination in the instant application.

Sequence Compliance

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and /or amino acid sequences set forth in CFR § 1.821(a)(1) and (a)(2): See, for example, page 31, lines 7 and 8, page 35, lines 20 and 21, page 36, line 19, page 37, lines 23 and 24, and page 41, line 10 . However, this application fails to comply with the requirements of CFR § 1.821 through 1.825 because it lacks any submission of a computer readable form sequence listing, a paper copy for the specification, a statement under CFR § 1.821(f) and (g), and SEQ ID numbers cited along with each sequence in the specification or Figures. Applicants are also reminded that SEQ ID numbers are not required in the Figures per se, however, the

corresponding SEQ ID numbers then are required in the Brief Description of the Drawings section in the specification. Applicants are also reminded that a CD_ROM sequence listing submission may replace the paper and computer readable form sequence listing copies. Applicants are given the same response time regarding this failure to comply as that set forth to respond to this office action. Failure to respond to this requirement may result in abandonment of the instant application or a notice of a failure to fully respond to this Office Action.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-18 and 20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 20 are generally narrative and indefinite, failing to conform with current U.S. practice. They appear to be a literal translation into English from a foreign document and are replete with grammatical and idiomatic errors. See for example claim 1, lines 1-4 which recites "a device including a substrate and a plurality of materials disposed on a surface of said substrate from said surface of said device", and claim 20 claim, lines, 2-4 which recites "a plurality of biologically-related materials disposed on a surface of said substrate from said surface". Clarification via clearer claim wording is

requested. Claims 2-18 are also included under this rejection due to their dependence from claim 1.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-18 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Arlinghaus et al. (IDS: Proceedings of the 12th International Conference of Secondary Ion Mass Spectrometry) taken in view of Pellin et al. (US Patent No. 6,137,110).

Arlinghaus et al. disclose the novel DNA sequencing method that utilizes TOF-SIMS (time-of-flight Secondary Ion Mass spectrometry) to characterize immobilized DNA and PNA molecules affixed to biosensor chips (acquiring information in relation to

a device including a substrate and a plurality of materials disposed thereon using time of flight secondary ion mass spectrometry). See Arlinghaus et al., page 951, Introduction, lines 1-20. The methodology of TOF-SIM involves the irradiation of various regions of samples affixed to a surface with a primary ion beam which generates charged secondary ions from the sample (irradiating primary ion beam on surface of said biochip). Mass analysis of said secondary ions is performed in a time of flight measurement procedure wherein a charge to mass ratio is established on the basis of the time it takes ions to pass through an electric or magnetic field of fixed strength (conducting mass-analysis of secondary ions via time of flight). The disclosed methodology of Arlinghaus et al. also involves preparing multiple samples immobilized on 5x5 mm^2 silicon wafers, termed "biosensor chips" (irradiating a pulsed primary ion beam on different positions of the surface of a biochip). See Arlinghaus et al., Title, page 951, Introduction, lines 1-20, and Experiment and Sample preparation, page 951, line 21 through page 95, line 5. The results of the TOF-SIM analysis of DNA and PNA samples are presented by Arlinghaus et al. as spectrograms containing two axes representing peak intensity and a mass to charge ratio (results obtained as two-dimensional information on the basis of said pattern of said irradiating pulsed primary ion beam). See Arlinghaus et al., Figure 2.

Arlinghaus et al. explored the homogeneity of the samples immobilized to chip surfaces through the TOF-SIM process and established a donut-shaped distribution to immobilized droplets. See Arlinghaus et al., page 953, line 6 through page 954, line 2, and Figure 5. Under a reasonably broad interpretation, in order to explore the potential

distribution of samples immobilized on a chip surface as disclosed in Arlinghaus et al., one of skill in the art must irradiate the surface of said chip in a pattern in order to determine what surface regions contain sample and what surface regions do not contain sample. The examiner has construed the above described procedure for determining the homology of a sample disposed on a surface to read on the claimed irradiating on different positions in a discontinuous pattern.

(regarding claim 2) Additionally, since Arlinghaus et al. demonstrated that the samples where predisposed to a symmetrical donut shape it is reasonable to conclude that the pattern of irradiation used to establish the surface features encompassed the region containing the entire sample surface area, which under a reasonably broad interpretation reads on the claimed discontinuous pattern is selected to be a two-dimensionally random pattern.

(regarding claims 3 and 5) Multiple samples immobilized on a biochip would necessarily involve the selected targeting of specific positions on said biochip and under a reasonably broad interpretation read on the claimed discontinuous pattern is selected to be a specifically programmed pattern and combination of scanning of the primary beam and positional scanning of said substrate.

(regarding claim 6) The disclosed methodology of Arlinghaus et al. involves preparing multiple samples immobilized on silicon wafers which are further termed "biochips" (the device is a chip on which biological-related materials are disposed). See Arlinghaus et al., Title, page 951, Introduction, lines 1-20, and Experiment and Sample preparation, page 951, line 21 through page 95, line 5.

(regarding claims 7-11) Arlinghaus et al. teaches that the disclosed TOF-SIM methodology can be used in the characterization of DNA, PNA, RNA, PNA-DNA duplexes, DNA duplexes, cDNA, and the identification of expressed genes (broadly construed as protein). See Arlinghauseet al., page 951, Introduction, lines 1-20.

(regarding claim 12) Arlinghaus et al. discloses that because the backbone of DNA contains phosphates and PNA does not, an analysis technique that identifies the presence of phosphates in a molecular surface layer would for the first time allow the use of genomic DNA for hybridization on a biosensor chip (secondary ion species generated by said primary ion beam includes at least species derived by the fragmentation and ionization of the phosphate backbone derived from nucleic acid). See Arlinghaus et al., page 951, Introduction, lines 11-14.

(regarding claim 13) The spectra presented by Arlinghaus et al. in Figure 2 clearly demonstrate the masses corresponding to PO_2^- and PO_3^- (wherein the secondary ion species generated by said primary ion beam includes at least any one of P^-, PO^-, PO_2^-, and PO_3^-).

(regarding claims 14 and 15) Arlinghaus et al. disclose in Figure 4 the signal intensity in recorded spectra related to T- and C- bases (secondary ion species derived by fragmentation and ionization of nucleic acid bases; at least any one of (adednine-H)$^-$, (thymine-H)$^-$, (guanine-H)$^-$, (cytosine-H)$^-$, and (uracil-H)$^-$).

(regarding claims 16 and 17) Arlinghaus et al. disclose in figure 2. the spectra resulting from TOF-SIMS analysis performed on PNA molecules that include peaks pertaining to side chains from the PNA samples immobilized on a chip surface (species

derived by fragmentation and ionization of peptide backbone). Using a reasonably broad interpretation, the side chain of the PNA molecules that are attached to the peptide backbone can be construed to read on the claims species derived by the ionization of amino acid residual group. See Arlinghaus et al, Figure 2 and page 952, lines 6-16.

(regarding claim 20) Arlinghaus et al. disclose that all TOF-SIM experiments in the reference were performed using a Poschenrieder-type TOF instrument and reads on the claimed apparatus for acquiring information in relation to a biochip including material disposed on a the surface of said biochip using time of flight secondary ion mass spectroscopy.

While Arlinghaus et al. discloses the above applications of TOF-SIM for the characterization of DNA and PNA related molecules affixed to the surface of a biosensor chip, Arlinghaus et al. does not fairly disclose or teach the use of the irradiation of a pulsed primary ion on different positions of a surface wherein said primary ion beam has a spot size (cross section) smaller than the area to be measured. Further, Arlinghaus et al. does not fairly disclose or teach the use of a primary ion beam wherein the ions are gold ions or carrying out measurements while a substrate is grounded.

Pellin et al. teaches a method and apparatus for applying a focused ion beam (FIB) sources that may serve as a significant improvement for Secondary Ion Mass spectrometers (SIMs). See Pellin et al., Abtract and column 1, lines 45-64. The FIB source disclosed provides a primary pulsed ion beam that also has an extremely narrow

cross section of submicron diameter (irradiating with a pulsed primary ion beam; spot size smaller than an area to be measured on a surface). See Pellin et al., Abstract and column 3, lines 45-61.

(regarding claim 4) Pellin et al. specifically disclose that the metal ion for the focused ion beam can be gold (Au). See Pellin et al., column 6, lines 4 and 5.

(regarding claim 18) Pellin et al. also disclose a preferred embodiment of the method and system wherein the ion extracting system is grounded (substrate is held in a condition of being electrically grounded). Further, the focused ion system disclosed by Pellin et al. is a reflection type apparatus. See for example Pellin et al., Figure 1 wherein a pulsed laser beam (14) is reflected off of a concave mirror (18) to produce metal ions.

Thus, taken in view of Pellin et al., it would have been obvious to one of skill in the art to employ the improved focused ion device for use in the TOF-SIM characterization of DNA and PNA biosensor chips as taught by Arlinghaus et al. as described above to result in the practice of the instantly claimed invention.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eric S. DeJong whose telephone number is (571) 272-6099. The examiner can normally be reached on 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, Ph.D. can be reached on (571) 272-0718. The fax phone

number for the organization where this application or proceeding is assigned is (571) 272-8300.

Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instrument Examiner, Tina Plunkett, whose telephone number is (571) 272-0549.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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Ardin H. Marschel 5/19/05
ARDIN H. MARSCHEL
PRIMARY EXAMINER